(FILE 'HOME' ENTERED AT 08:08:22 ON 23 DEC 2003)

FILE 'REGISTRY' ENTERED AT 08:08:32 ON 23 DEC 2003

L1 1 S 50-28-2/RN

FILE 'USPATFULL' ENTERED AT 08:09:02 ON 23 DEC 2003

L2 1086 S L1

L3 604 S L2 AND PD<2001

L4 89 S L3 AND OSTEOPOROSIS

L5 0 S L4 AND (ESTRADIOL (P) OSTEOPROSIS)

L6 34 S L4 AND (ESTRADIOL (P) OSTEOPOROSIS)

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN **50-28-2** REGISTRY
CN Estra-1,3,5(10)-triene-3,17-diol (17.beta.)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Estradiol (8CI)
OTHER NAMES:
CN (+)-3,17.beta.-Estradiol
CN .beta.-Estradiol
CN 13.beta.-Methyl-1,3,5(10)-gonatriene-3,17.beta.-ol
CN 17.beta.-Estradiol
CN 17.beta.-Oestradiol
CN 3,17-Epidihydroxyestratriene
CN 3,17.beta.-Dihydroxyestra-1,3,5(10)-triene
CN 3,17.beta.-Estradiol
CN Aerodiol
CN Altrad
CN Aquadiol
CN Bardiol
CN Beta-estradiol
CN Climaderm
CN Climara
CN Compudose
CN Compudose 200
CN Compudose 365
CN Corpagen
CN Dermestril
CN Dihydrofollicular hormone
CN Dihydrofolliculin
CN Dihydromenformon
CN Dihydrotheelin
CN Dihydroxyestrin
CN Dimenformon
CN Diogyn
CN Diogynets
CN Divigel
CN E 2
CN Encore
CN Epiestriol 50
CN Estra-1,3,5(10)-triene-3,17-diol, (17.beta.)-
CN Estra-1,3,5(10)-triene-3,17.beta.-diol
CN Estrace
CN Estraderm
CN Estraderm TTS
CN Estraderm TTS 100
CN Estraderm TTS 50
CN Estradot
CN Estraldine
CN Estring Vaginal Ring
CN Estroclim
CN Estroclim 50
CN Estrogel
CN Estrovite
CN Evorel
CN Femanest
CN Femestral
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS STEREOSEARCH
MF C18 H24 O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM,

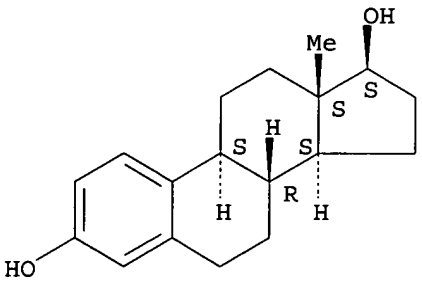
CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSDRUGNEWS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL, VETU

(*File contains numerically searchable property data)

Other Sources: EINECS**, WHO

(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

50684 REFERENCES IN FILE CA (1907 TO DATE)
851 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
50748 REFERENCES IN FILE CAPLUS (1907 TO DATE)
12 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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L6 ANSWER 26 OF 34 USPATFULL on STN
AN 92:12940 USPATFULL
TI Pharmaceutical compositions for nasal administration containing steroid hormones and dimethyl-.beta.-cyclodextrin
IN Hermens, Walter A. J. J., Thorbeckestraat 80, 6136 DD Sittard, Netherlands
Merkus, Franciscus W. H. M., Mozartlaan 7, 3723 JL Bithoven, Netherlands
PI US 5089482 19920218 <--
AI US 1989-372917 19890628 (7)
PRAI NL 1988-1670 19880701
DT Utility
FS Granted
EXNAM Primary Examiner: Griffin, Ronald W.; Assistant Examiner: Carson, Nancy S.
LREP Cooper & Dunham
CLMN Number of Claims: 30
ECL Exemplary Claim: 1,15
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 5089482 19920218 <--
SUMM The invention accordingly relates to pharmaceutical compositions for the nasal administration of the natural female sex hormones 17.beta.-**estradiol** and progesterone with an increased absorption of the hormones referred to by combination with the adjuvant dimethyl-.beta.-cyclodextrin. Examples of dosage forms of 17.beta.-**estradiol** and/or progesterone suitable for nasal administration are solutions, suspensions, gels and ointments. The dosage forms containing the hormones referred to,. . . separately or in combination, can be used, for example, in treating or preventing postmenopausal conditions, such as vasomotor symptoms and **osteoporosis**.
IT **50-28-2**, 17.beta.-Estradiol, biological studies 57-83-0, Progesterone, biological studies
(nasal compns. contg. dimethylcyclodextrin and)

L6 ANSWER 5 OF 34 USPATFULL on STN
AN 2000:164095 USPATFULL
TI Preparation with an acrylic-based, adhesive copolymeric matrix for the transdermal delivery of estradiol
IN Rovati, Luigi, Monza, Italy
Rovati, Lucio, Monza, Italy
Makovec, Francesco, Monza, Italy
Cordes, Gunter, Leichlingen, Germany, Federal Republic of
Fischer, Wilfried, Bad Tolz, Germany, Federal Republic of
PA Rotta Research Laboratorium S.p.A., Monza, Italy (non-U.S. corporation)
PI US 6156335 20001205 <--
WO 9310772 19930610 <--
AI US 1994-244132 19940715 (8)
WO 1992-EP2704 19921124
19940715 PCT 371 date
19940715 PCT 102(e) date
PRAI IT 1991-TO907 19911125
DT Utility
FS Granted
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Ghali, Isis
LREP Pitney, Hardin, Kipp & Szuch, LLP
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 572
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6156335 20001205 <--
WO 9310772 19930610 <--
SUMM Ovarian secretion of 17.beta.-**estradiol** is lacking in postmenopausal women. In many women this physiological phenomenon induces progressive hypotrophy of the urogenital system as well as characteristic vasomotor symptoms, often followed by **osteoporosis** affecting particularly the vertebral column.
IT **50-28-2**, 17.beta.-Estradiol, biological studies
(transdermal delivery system for, as skin patch)

L6 ANSWER 6 OF 34 USPATFULL on STN
AN 2000:149740 USPATFULL
TI Transdermal therapeutic system containing estradiol
IN Meconi, Reinhold, Neuwied, Germany, Federal Republic of
Seibertz, Frank, Bad Honningen/Ariendorf, Germany, Federal Republic of
Horstmann, Michael, Neuwied, Germany, Federal Republic of
Lichtenberger, Rainer, Darmstadt, Germany, Federal Republic of
PA LTS Lohmann Therapie-Systeme GmbH, Neuwied, Germany, Federal Republic of (non-U.S. corporation)
Merck Patent GmbH, Darmstadt, Germany, Federal Republic of (non-U.S. corporation)
PI US 6143319 20001107 <--
AI US 1997-961039 19971030 (8)
RLI Continuation of Ser. No. US 545703
PRAI DE 1993-4314970 19930506
DE 1993-4336557 19931027
DT Utility
FS Granted
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Howard, S.
LREP Wenderoth, Lind & Ponack, L.L.P.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 564
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI US 6143319 20001107 <--

SUMM . . . diseases, transdermal therapeutic systems (TTS) have been introduced on the market. Also, transdermal therapeutic systems containing the estrogenic active substance 17-.beta.-**estradiol** used as therapeutic agent for climacteric complaints and--for some time now--against **osteoporosis** are commercially available and show good therapeutic results.
IT **50-28-2**, Estradiol, biological studies
(adhesive for estradiol-contg. transdermal therapeutic system)

L6 ANSWER 7 OF 34 USPATFULL on STN
AN 2000:138405 USPATFULL
TI Treatment of **osteoporosis** and metabolic bone disorders with nitric oxide substrate and/or donors
IN Yallampalli, Chandrasekhar, Houston, TX, United States
Wimalawansa, Sunil J., Friendswood, TX, United States
PA Board of Regents, The University of Texas System, United States (U.S. corporation)
PI US 6133320 20001017 <--
AI US 1998-177978 19981022 (9)
RLI Division of Ser. No. US 1996-616470, filed on 19 Mar 1996, now patented, Pat. No. US 5898038
DT Utility
FS Granted
EXNAM Primary Examiner: Criares, Theodore J.
LREP Fulbright & Jaworski
CLMN Number of Claims: 98
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 794
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Treatment of **osteoporosis** and metabolic bone disorders with nitric oxide substrate and/or donors
PI US 6133320 20001017 <--
AB Primary and secondary **osteoporosis** in a female or a male mammal is treated by administering thereto a nitric oxide synthase substrate, a nitric oxide. . . other medications as described above can be used in both women and men, (preferably human) for prevention and treatment of **osteoporosis** and other metabolic bone disorders.
SUMM This invention relates to a new method for treatment of **osteoporosis** and bone mineral disorders and to prevent bone loss, fractures and other abnormal clotting patterns, urogenital discomfort, prevention and treatment. . . and/or a progestin. Same compounds are also useful in men to decrease bone turnover and hence prevention and treatment of **osteoporosis** and for treatment of other metabolic bone disorders.
SUMM This invention is also applicable to both primary and secondary **osteoporosis** in both females and males. In the female, the method of choice of treatment of primary **osteoporosis** is estrogen replacement therapy and in the case of male, the method of choice of treatment of primary **osteoporosis** is androgen replacement therapy. In both sexes for the secondary **osteoporosis** the underlying causative factors are numerous, including medication-induced **osteoporosis** (e.g., corticosteroids, antiepileptics, anticoagulants, thyroxine), immunosuppressant agents used in prevention of graft rejection and other disorders (cyclosporin), malignancies (e.g., multiple. . .
SUMM One aspect of the present invention provides a method for the prevention and treatment of primary and secondary **osteoporosis**, including medication induced-**osteoporosis** (i.e. corticosteroid-induced **osteoporosis**) and other metabolic bone disorders with a nitric oxide substrate and/or donor.
SUMM . . . a progestational agent is used in combination with a nitric oxide substrate and/or donor for the prevention and treatment of **osteoporosis** and other metabolic bone disorders.

SUMM It is a further object to provide a method for the prevention and treatment of **osteoporosis** and other metabolic bone disorders using an estrogenic agent in combination with a nitric oxide substrate and/or donor.

SUMM It is another object to provide a method for prevention and treatment of **osteoporosis** and other metabolic bone disorders using a combination of an estrogenic agent and progestational agent with a nitric oxide substrate. . .

SUMM Another object is to provide a method of prevention and treatment of male primary and secondary **osteoporosis** and other metabolic bone disorders using nitric oxide substrate and/or donor.

SUMM . . . which this invention pertains. Another object is to provide a method of prevention and treatment of male primary and secondary **osteoporosis** and other metabolic bone disorders using nitric oxide substrate and/or donor.

SUMM An important embodiment of this invention relates to a method of treating **osteoporosis** or other metabolic bone disorders in a menopausal or postmenopausal female. This embodiment comprises administering to a female manifesting the. . . alone or in further combination with one or more of an estrogen, and a progestin in amounts effective to ameliorate **osteoporosis** symptoms. The amount of the estrogen is bioequivalent to approximately 2 mg per day of **estradiol** and the amount of the progestational agent administered is bioequivalent to 50-300 mg of injected progesterone. The amount of the. . . donor). This invention also relates to use of L-arginine or nitric oxide donor compounds in prevention and treatment of primary **osteoporosis** in men and in both sexes, secondary **osteoporosis**, including medication-induced **osteoporosis** (e.g., corticosteroid-induced **osteoporosis**) and other metabolic bone disorders. L-arginine is the only acknowledged substrate of nitric oxide synthase but any analogous substrates behaving. . .

DETD The methods of this invention to treat **osteoporosis** and other bone mineral disorders in a menopausal/postmenopausal manunal and in men, preferably a human, who is manifesting the signs and/or symptoms or both (i.e. treatment of **osteoporosis**) thereof or who is a high risk candidate (prevention of **osteoporosis**) for doing so, e.g., as determined by appropriate clinical conditions.

DETD In the case of female, for both primary and secondary **osteoporosis** an added effect is achieved when the nitric oxide substrate and/or nitric acid donor is administered concurrently with an estrogen. . .

DETD In the case of a male, for both primary and secondary **osteoporosis**, an added effect is achieved when the L-arginine and/or nitric oxide donor is administered concurrently with an androgen. Thus, the. . .

DETD Surgical or natural menopause in women leads to both cortical and trabecular bone loss (S. J. Wimalawansa, 1993). **Osteoporosis** induced by OVX in rats has been widely used as a model of postmanopausal **osteoporosis** (D. N. Kalu, 1991) and has been validated as a clinically relevant model of human postmenopausal bone loss (Wronski et. . . . likely that the E.sub.2 -induced increase in BMD is dependent upon NO generation, since L-NAME completely obliterated the effects of **estradiol**. These studies indicate that exogenous NO can reverse the bone loss in **estradiol**-deficit animals and that **estradiol**-induced increase in BMD may be NO dependent.

DETD Treatment of **Osteoporosis** and Other Metabolic Bone Disorders

DETD To a nonpregnant human female (ca 45 years; 50-80 kg) displaying the signs of menopause or postmenopausal **osteoporosis** (primary and secondary) and/or other metabolic bone disorders, or to a human male displaying signs of **osteoporosis** and/or other metabolic bone disorders, administer L-arginine initially with a dose range of 0.5 to 20 g of L-arginine per. . .

DETD Treatment of **Osteoporosis** and Other Metabolic Bone Disorders

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DETD Treatment of **Osteoporosis** and Other Metabolic Bone Disorders
DETD Treatment of **Osteoporosis** and Other Metabolic Bone Disorders
DETD Treatment of **Osteoporosis** and Other Metabolic Bone Disorders
CLM What is claimed is:
1. A method for prevention or treatment of primary and secondary **osteoporosis** of a female or male mammal comprising administering to the susceptible or afflicted mammal at least one of L-arginine effective. . .
6. The method of claim 1, wherein the mammal is a female human suffering from primary or secondary **osteoporosis**.

7. The method of claim 1, wherein the mammal is a female human subject to hormone replacement therapy, a candidate for hormone replacement therapy or for **osteoporosis** therapy.

8. The method of claim 1 wherein the mammal is a male human having **osteoporosis** or being a candidate for **osteoporosis** therapy.

51. A method for prevention or treatment of primary and secondary **osteoporosis** comprising administering a nitric oxide donor in an amount effective to provide a level of nitric oxide donor of about 1-1000 nM to a female or male mammal susceptible to or suffering from primary or secondary **osteoporosis**.

56. The method of claim 51, wherein the mammal is a female human suffering from primary or secondary **osteoporosis**.

57. The method of claim 51, wherein the mammal is a female human subject to hormone replacement therapy, a candidate for hormone replacement therapy or for **osteoporosis** therapy.

58. The method of claim 51, wherein the mammal is a male human having **osteoporosis** or being a candidate for **osteoporosis** therapy.

IT 50-27-1, Estriol **50-28-2**, 17.beta.-Estradiol, biological studies 53-16-7, Estrone, biological studies 55-63-0, Nitroglycerin 57-83-0, Progesterone, biological studies 58-22-0, Testosterone 68-22-4, Norethisterone 87-33-2, Isosorbide dinitrate 152-62-5, Dydrogesterone 360-70-3, Nandrolone decanoate 520-85-4, Medroxyprogesterone 797-63-7, Levonorgestrel 979-32-8, Estradiol valerate 1406-16-2D, Vitamin D, metabolites 6533-00-2, Norgestrel 7414-83-7, Disodium etidronate 7440-70-2D, Calcium, compds., biological studies 7681-49-4, Sodium fluoride, biological studies 9007-12-9, Calcitonin 10596-23-3 13598-36-2D, Phosphonic acid, alkylidenebis-, derivs. 14402-89-2, Sodium nitroprusside 16051-77-7, Isosorbide mononitrate 16984-48-8, Fluoride, biological studies 33876-97-0, SIN-1 40391-99-9 61912-98-9, Insulin-like growth factor 66376-36-1, Alendronate 105462-24-6, Risedronic acid 106602-62-4, Amylin 114084-78-5, Ibandronate
(treatment of osteoporosis and metabolic bone disorders with nitric oxide substrate and/or donors)

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     (FILE 'HOME' ENTERED AT 08:08:22 ON 23 DEC 2003)

     FILE 'REGISTRY' ENTERED AT 08:08:32 ON 23 DEC 2003
L1             1 S 50-28-2/RN

     FILE 'USPATFULL' ENTERED AT 08:09:02 ON 23 DEC 2003
L2          1086 S L1
L3           604 S L2 AND PD<2001
L4            89 S L3 AND OSTEOPOROSIS
L5             0 S L4 AND (ESTRADIOL (P) OSTEOPROSIS)
L6            34 S L4 AND (ESTRADIOL (P) OSTEOPOROSIS)
L7           716 S CONJUGATED (P) ESTRADIOL
L8           301 S L7 AND PD<2001
L9            70 S L8 AND L1
L10           17 S L9 AND OSTEOPOROSIS
L11            9 S CONJUGATED (W) (ESTRONE OR EQUILIN OR DEHYDROESTRONE OR ESTRA
L12            6 S L11 AND PD<2001
L13            0 S L12 AND OSTEOPORPSIS
L14            1 S L12 AND OSTEOPOROSIS
L15            0 S CONJUGATED (W) EQUILIN

     FILE 'REGISTRY' ENTERED AT 08:46:53 ON 23 DEC 2003
L16            1 S EQUILIN/CN
L17            0 S (CONJUGATED EQUILIN)/CN
L18            1 S PREMARIN/CN
L19            0 S (EQUILIN,CONJUGATED)/CN

     FILE 'USPATFULL' ENTERED AT 08:48:41 ON 23 DEC 2003
L20            8 S L11 NOT L14
L21         5289 S CONJUGATED/AB

     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT,
     CAPLUS, CEN, DISSABS, DGENE, DRUGB, DRUGMONOG2, IMSDRUGNEWS, DRUGU,
     EMBAL, EMBASE, ESBIOBASE, IFIPAT, IMSPRODUCT, IPA, JICST-EPLUS, KOSMET,
     LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, ...' ENTERED AT 08:56:46 ON
     23 DEC 2003
L22        222759 S CONJUGATED/AB
L23          1916 S L22 AND (ADVANTAGE OR ADVANTAGEOUS OR ADVANTAGEOUSLY)/AB
L24            57 S L23 AND (ESTROGEN OR ESTROGENIC)/AB
L25            34 S L24 AND PD<2001

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L18 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 12126-59-9 REGISTRY *
* Use of this CAS Registry Number alone as a search term in other STN files may result in incomplete search results. For additional information, enter HELP RN* at an online arrow prompt (=>).
CN Estrogens, conjugates (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Estrogens, conjugated
OTHER NAMES:
CN Ayerogen
CN Ayerogen Crema Vaginal
CN Azumon
CN C.E.S.
CN Cenestin
CN Climarest
CN Conjugated estrogens
CN Conjugates, estrogens
CN Conjugen
CN Dagynil
CN Emopremarin
CN Equin
CN Femavit
CN Hyphorin
CN Mannest
CN Menopak E
CN Menpoz
CN Neo-Menovar
CN Oestro-Feminal
CN Ovest
CN Premaril
CN **Premarin**
CN Premarin Crema V
CN Premarin Creme
CN Premarin Vaginal Creme
CN Premarina
CN Premarose
CN Presomen
CN Prevagin-Premaril
CN Romeda
CN Sefac
CN Srogen
CN Sukingpo
CN Transannon
DEF A complex mixture of sodium estrone sulfate and sodium equilin sulfate derived synthetically from estrone and equilin from horse urine. It may contain not less than 50% and not more than 60% sodium estrone sulfate and not less than 22.5% and not more than 32.5% sodium equilin sulfate.
MF Unspecified
CI MAN, CTS
LC STN Files: ADISNEWS, AGRICOLA, BIOSIS, CHEMLIST, CIN, DDFU, DIOGENES, DRUGU, IMSCOSEARCH, MSDS-OHS, RTECS*, TOXCENTER, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

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